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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,356	02/05/2004	Leslie P. Weiner	23714-07992	6800

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 12/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/773,356	WEINER ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9,11-19 and 23-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 8, 9, 11-19 and 23-30 are pending and under examination.

2. Applicant's amendment and remarks, filed 9/22/05, are acknowledged. In view of Applicant's amendment, the previous rejections under the second paragraph of 35 U.S.C. 112, and the first paragraph of 35 U.S.C. 112 (for lack of enablement), have been withdrawn.

3. The specification stands objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

The method of Claims 8, 26, and 28 wherein natural and/or synthetic myelin proteins are employed, has no antecedent basis in the specification.

The specification must be amended to include said limitations.

Applicant argues that support for the limitations can be found at pages 8 and 10 of the specification. The specification discloses only PBMCs cultured with cow myelin proteins or synthetic complete human myelin (page 8), or human PBMCs cultured with bovine total myelin proteins (page 10). The generic T cells cultured with generic natural or synthetic myelin proteins are not disclosed.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 24, 25, and 30 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of:

A) The method of Claim 24 comprising at least two of MBP, MOG, PLP, and MAG.
B) The method of Claim 25 comprising at least MBP, MOG, PLP, and MAG.
C) The method comprising the specific steps set forth in Claim 30.

Applicant's arguments, filed 9/22/05 have been fully considered but they are not persuasive. Applicant argues that the disclosure of "a plurality of myelin proteins", "synthetic complete human proteins", and "cow (bovine) myelin proteins" supports the limitations of the claims as these proteins would include MBP, MOG, PLP, and MAG.

Applicant is advised that generic disclosures of myelin proteins do not support the individual components of said proteins that are now claimed, i.e., the disclosure of a genus is insufficient support for individual species comprising said genus unless the number of species is sufficiently small that all are readily envisioned by the skilled artisan. In the instant case it has not been established that all species of proteins comprising generic myelins are even known, much less limited and readily envisioned by the skilled artisan.

Note that Applicant has not addressed the rejection of part C) above.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 8, 9, 11, 12, 14 and 15 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Stinissen et al. (1996).

As set forth previously, Stinissen et al. teaches a method of mediating an immune response comprising administering irradiation-attenuated T-cells derived from autologous peripheral mononuclear cells (comprising T cells) cultured in the presence of natural or synthetic myelin proteins (see particularly page 503, T CELL VACCINATION IN MS).

Applicant's arguments, filed 9/22/05 have been fully considered but they are not persuasive. Applicant argues that the original claims recited methods of administering to humans T cells that have been cultured in the presence of (claim 10) and are reactive with (claim 11) multiple myelin proteins, e.g., at least two myelin proteins, e.g., MBP and MOG, or e.g., a mixture of all myelin protein, e.g., bovine myelin proteins.

Applicant is advised that the claims do not comprise the limitations set forth by Applicant in the instant arguments. They did not, and still do not, recite a method employing multiple myelin proteins and, in particular, they did not, and still do not, recite a method employing multiple different myelin proteins. Accordingly, the reference which teaches the use of myelin, which is natural or synthetic, (of which more than 1 molecule was employed in the method of the reference), meets the limitations of the claims.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 16-19 are rejected under 35 U.S.C. 103(a) each as being unpatentable over Stinissen et al. (1996).

As set forth previously, Stinissen et al has been discussed above. The reference differs from the claimed invention only in that it does not teach the optimization of the claimed method as set forth in dependent Claims 16-19. For example, the choice of dosage (Claim 17), and timing (Claim 16), would have fallen well within the purview of the skilled artisan at the time of the invention. Regarding the increasing of the dosages as set forth in Claims 18 and 19, one of ordinary skill in the art at the time the invention was made would have been well aware of the concept of increasing dosage if no response is obtained up to the point of efficacy or adverse reaction. These limitations do not render the claimed method patentably distinct.

Applicant's arguments, filed 9/22/05 have been fully considered but they are not persuasive. Applicant again argues that the reference does not teach the use of multiple myelin proteins.

See the Examiner's response to the argument regarding this unclaimed limitation in Section 7 above.

10. Claim 13 stands rejected under 35 U.S.C. 103(a) each as being unpatentable over Stinissen et al. (1996) in view of Correale et al (1995).

As set forth previously, Stinissen et al. has been discussed above. The reference further teaches that MBP is not the only autoantigen candidate in MS. The reference teaches that additional antigens, including PLP, MAG, and MOG might also be the targets of autoreactive T cells (see particularly page 501, column 1, second full paragraph).

The reference differs from the claimed invention only in that it does not teach the use of attenuated T cells that target more than one myelin protein.

Correale et al. extends the teachings of Stinissen et al. regarding additional MS autoantigens. The reference teaches that as MS develops, myelin breakdown exposes additional myelin antigens (besides MBP) to autoreactive T cells, thus, broadening the autoimmune response (see particularly page 1375, last paragraph - page 1376, first paragraph.

From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform the method of administering attenuated T cells, as taught by Stinissen et al., employing attenuated T cells autoreactive to multiple myelin antigens. One of ordinary skill in the art at the time the invention was made would have been motivated to employ attenuated T cells autoreactive to multiple myelin antigens given the teachings of Stinissen et al. that MBP is not the only autoantigen candidate in MS and extended by Correale et al. that as MS develops, myelin breakdown exposes additional myelin antigens (besides MBP) to autoreactive T cells, thus broadening the autoimmune response.

Applicant's arguments, filed 9/22/05 have been fully considered but they are not persuasive. Applicant argues that the combined references do not meet the limitations of the claims, in particular, Correale et al. does not teach all of the limitations of the claimed method, e.g., vaccination with attenuated T cells. Applicant further argues that the cited art provides no motivation to combine the teachings of the references.

Applicant is advised that if the Correale et al. reference had taught vaccination with attenuated T cells specific for the multiple MS antigens of the of the reference, MBP, MAG, PLP, and MOG, the rejection would have been under 35 U.S.C. 102. It appears that Applicant has missed the point of combining references; in this case taking the method of the primary reference, Stinissen et al., and improving the method in a way which would have been obvious to the ordinarily skilled artisan at the time of the invention by employing attenuated T cells

specific for the multiple antigens of the secondary reference, Correale et al., to achieve superior results. Further, in arguing the requirement for an obviousness-type rejection, Applicant has failed to note that motivation to combine references may be found in the knowledge generally available to one of ordinary skill in the art (MPEP 2143.01), i.e., the motivation to combine references need not be found explicitly, nor even implicitly, in the references themselves. Clearly, if a method of treatment employing attenuated T cells versus one MS antigen was known in that art, and if additional MS antigens were also known, it would have taken no great insight to employ attenuated T cells versus those additional MS antigens also to provide a superior treatment.

Applicant asserts a lack of expectation of success.

Applicant's assertion alone fails to comprise a convincing argument. Stinissen et al. report promising and encouraging results, thus, it would seem that an improved method of treatment would show results at least as good. Additionally, this seems like a curious argument given the minimal teachings of the specification wherein anecdotal results obtained from just four patients show that the best results achieved were a lack of change, and Applicant refers to this (in the instant arguments) as a showing of effective treatment.

Applicant argues unexpected results, in particular, Applicant points out the teachings of Stinissen et al. regarding a lack of significant clinical improvement regarding disease scores and MRI of brain lesions, while asserting a showing of effective treatment in the instant application.

It must be noted that the instant application also specifically discloses a lack of significant clinical improvement (i.e., no change as reported here comprises a lack of improvement) regarding disease scores, while changes in MRI of brain lesions are not addressed. Yet Applicant refers to the instant results as a showing of effective treatment. This would appear to be an inconsistent argument.

Applicant argues that the instant method meets a long-felt but unresolved need.

Applicant is advised that the minimal disclosure, comprising only anecdotal and uncontrolled data, does not establish an effective treatment for MS and cannot be said to satisfy a long-felt need nor demonstrate success where others have failed as is asserted by Applicant.

Applicant concludes by asserting that, "Applicant has demonstrated clinical improvement in MS patients where Zhang has failed".

Applicant is advised that no such demonstration of improvement has been presented in this application.

11. No claim is allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the

Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

12/10/05

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